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(21) International Application Number: PCT/EP95/03861 (22) International Filing Date: 28 September 1995 (28.09.95) (30) Priority Data: 9419715.9 30 September 1994 (30.09.94) GB (71) Applicant (for all designated States except US): THE BOOTS COMPANY PLC [GB/GB]; 1 Thane Road West, Nottingham NG2 3AA (GB). (72) Inventors; and (75) Inventors/Applicants (for US only): BARTON, Stephen, Peter [GB/GB]; The Boots Company plc, 1 Thane Road West, Nottingham NG2 3AA (GB); GALLEY, Edward [GB/GB]; The Boots Company plc, 1 Thane Road West, Nottingham NG2 3AA (GB). (74) Agent: KIRK, Martin, John; The Boots Company plc, Patents Dept., R4 Pennyfoot Street, Nottingham NG2 3AA (GB).		(81) Designated States: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT, UA; UG, US, UZ, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG), ARIPO patent (KE, MW, SD, SZ, UG). Published <i>Without international search report and to be republished upon receipt of that report.</i>
(54) Title: HAIR STIMULANT COMPOSITION (57) Abstract <p>The invention provides the use of one or more of the following substances as hair stimulants: 1) a water-soluble potassium, copper and/or zinc salt, suitably being an acetate salt; 2) a flavone or flavone derivative, suitably comprising rutin, such as troxerutin; 3) a xanthine, such as a theophylline, or a derivative thereof, such as methyl silanol theophyllin acetate alginate; 4) a mucopolysaccharide or derivative thereof such as dimethylsilanol hyaluronate; 5) a fat soluble vitamin or a derivative thereof such as vitamin A (retinol) palmitate or vitamin E (tocopherol); 6) Zedoary, ginger, and/or cinnamon oil; or combinations of these; 7) an allyl-based plant extract such as onion or garlic extract, such as onion extract in coconut oil or garlic extracted in butylene glycol.</p>		

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HAIR STIMULANT COMPOSITION

The present invention relates to a composition for use as a hair stimulant, to a method of modifying hair growth and/or hair loss, and to uses of substances
5 and/or compositions as hair stimulants.

The term "hair stimulant" as used herein means a substance or composition which either stimulates hair growth and/or inhibits hair loss in humans, especially on the scalp.

10 Loss of scalp hair is a normal phenomenon which occurs when the hair follicle comes to the end of its growth phase and enters a resting phase before re-starting the growth cycle. On the human scalp, follicles are not growing synchronously and around 10%
15 will be in the resting (telogen) phase at any one time. Thus normal loss will cause no noticeable alteration in scalp hair coverage. The normal ageing process sees an increase in the number of telogen follicles and results in the thinning of hair. The process is more pronounced
20 in males, leading to the largely accepted theory that the male hormone testosterone and its more active metabolite 5 α -dihydrotestosterone have a role in what is known as male pattern baldness.

Ageing is not the only cause of hair loss. It can
25 also have pathological causes, as in the condition known as alopecia areata, with a variety of clinical presentations and prognoses in which autoimmunity is thought to play a part. Hair loss may also occur in a number of other circumstances, such as when a patient is
30 treated with cytotoxic drugs or undergoes radiotherapy.

Some drugs are known to stimulate hair growth. An example is the drug minoxidil which, although originally developed as an antihypertensive, subsequently became a product (marketed under the Trade Name "Regaine") used with some success in promoting new hair growth.

There remains a need, however, for further means of stimulating hair growth and/or inhibiting hair loss.

According to the present invention, there is provided the use of one or more of the following substances ("the substances listed") as hair stimulants:

- 1) A water-soluble potassium, copper and/or zinc salt, suitably being an acetate salt;
- 2) A flavone or flavone derivative, suitably comprising rutin, such as troxerutin;
- 15 3) A xanthine, such as a theophylline, or a derivative thereof, such as methyl silanol theophyllin acetate alginate;
- 4) A mucopolysaccharide or derivative thereof such as dimethylsilanol hyaluronate;
- 20 5) A fat soluble vitamin or a derivative thereof such as vitamin A (retinol) palmitate or vitamin E (tocopherol);
- 6) Zedoary, ginger, and/or cinnamon oil; or combinations of these;
- 25 7) An allyl-based plant extract such as onion or garlic extract, such as onion extract in coconut oil or garlic extracted in butylene glycol.

Suitably, at least two, preferably at least three or more of the substances listed are used together, either simultaneously or sequentially.

- There is also provided the use of any one, preferably two or three, of the substances listed in the manufacture of a medicament for the treatment of hair loss, such as alopecia areata.

- There is further provided a method of treating hair loss (such as alopecia areata) by applying a flavone, a xanthine such as theophylline or a derivative thereof and at least one, suitably at least two of the other substances listed to the scalp. The substances may be applied either simultaneously or sequentially, but simultaneous application is preferred. The method may be used for medical and/or cosmetic purposes.

- The invention further provides a composition for stimulating hair growth and/or inhibiting hair loss in humans, comprising a flavone, a xanthine such as theophylline or a derivative thereof and at least one, suitably at least two of the other substances listed, for simultaneous or sequential administration to the scalp.

The substances listed are suitably included in compositions to the following concentrations (all w/w%)

- 1) 0.01 to 0.5%, suitably about 0.05%;
2) 0.01 to 0.5%, suitably about 0.1%;
3) 0.1 to 5%, suitably about 1%;
4) 0.1 to 5%, suitably about 1%;
5) 0.01 to 1%, suitably about 0.05%;
6) 0.1 to 5%, suitably about 0.5%; and
7) 0.01 to 1%, suitably about 0.1%

respectively wherein the numbering corresponds to the numbering used above.

The composition may comprise said components either in the form of a mixture, or in a physically separate state either for admixture prior to simultaneous application or for separate/sequential application to the scalp.

Suitably, the composition may be in the form of a shampoo, conditioner, hair gel, styling gel, hair cream or lotion, hair mousse, hairspray or hair lacquer.

It will be understood that further components may be added to the composition as is well-known in the art.

For example, preservatives may be present, such as bronopol, benzyl alcohol, imidazolidinyl urea, methyl paraben, propyl paraben, and naturally occurring preservatives such as the enzyme lactoperoxidase, particularly the blend of lactoperoxidase, glucose, glucose oxidase, iodide and thiocyanate marketed by The Boots Company PLC under the Trade Name "Myavert-C". Suitably such preservatives are included in an amount of from about 0.01% to about 2% by weight of the composition.

Styling gels may comprise resins such as polyvinyl pyrrolidone in a Carbopol gel and D-panthenol and/or propylene glycol as a conditioning aid.

Thickeners and viscosity modifying agents may be present, such as 1,3-butylene glycol, quaternised methyl-hydroxycellulose, amine oxides, block polymers of ethylene oxide and propylene oxide (for example, those available from BASF Wyandotte under the Trade Name

"Pluronic"), polyvinyl alcohols and fatty alcohols, suitably in an amount of from about 0.5% to about 10% by weight of the composition.

- 5 Surfactants may be present, such as silicone glycol copolymer, anionics such as sodium laurylether sulphates, amphoterics such as cocoa amidopropyl betaines, sarcosinates and sulphosuccinates.

- 10 Conditioning agents include proteins, protein hydrolysates, for example the blend of soya amino acids available from Croda Chemicals under the Trade Name "Hydrosoy 2000"; clays, for example the montmorillonite clay available from English China Clays under the Trade Name "Gel White HNF"; and quaternary ammonium compounds such as Dehyquart A.

- 15 Sequestering agents may be present, such as ethylenediamine tetraacetic acid and salts thereof, suitably in an amount of from about 0.005 % to about 0.5% by weight of the composition.

- 20 Perfumes may be present, suitably in an amount of from about 0.01% to about 2%, as may water soluble dyes such as tartrazine, suitably in an amount of from about 0.00001% to about 0.1% by weight of the composition.

- 25 The composition may be buffered by means well known in the art, for example by use of buffer systems comprising succinic acid, citric acid, lactic acid, phosphoric acid, mono- or disodium phosphoric and sodium carbonate. Suitably, the composition may have a pH between about 3 and about 10, preferably between about 4 and about 6.

The composition may also include an antidandruff agent such as salicyclic acid or zinc pyrithione suitably in an amount of from about 0.1% to about 5% by weight.

- 5 Cosmetic components, such as D-panthenol, henna extracts, soya amino acids and fruit extracts may be included as is well known in the art.

The invention will be understood with reference to the following non-limiting example:

Example 1 Hair stimulant composition

A hair stimulant composition was prepared as follows:

	<u>Component</u>	<u>Concentration</u> (w/w%)
5	Potassium acetate	0.10
	Copper (II) acetate	0.05
	Zinc acetate	0.05
	Troloxerutin	0.10
10	Methyl silanol theophyllin acetate alginate (available from Exsymol Ltd under the Trade Name "Theophyllisilane C")	1.00
	Dimethyl silanol hyaluronate (available from Exsymol Ltd under the Trade Name "DSH C")	1.00
15	D-Panthenol	0.50
	Silicone Glycol Copolymer (available from Dow Corning under the Trade Name "Dow Corning 193")	1.50
20	Mixture of Zedoary, ginger and cinnamon oil (available from VEVY under the Trade Name "Zedomina")	0.50
	Vitamin A palmitate	0.05
	Vitamin E (available from Henkel under the Trade Name "Copherol F1300")	0.05
25	Cyclomethicone 100 centistoke silicone fluid	1.00
	1,3-butylene glycol	5.00
	Quaternised methyl hydroxycellulose (available from Courtaulds under the Trade Name "DP969")	0.50
30	Soya amino acids (available from Croda Chemicals under the Trade Name "Hydrosoy 2000")	0.25
	Onion extract and coconut oil (available from VEVY under the Trade Name "Allum Cepa")	0.10
35		

METHOD OF PREPARATION

1. Oil soluble components - Zedoary extracts, onion extract, vitamin A palmitate, vitamin E and silicone glycol copolymer, were mixed with gentle heat.
2. Aqueous components were separately mixed with simple stirring in the following order - inorganic salts, flavonoid, theophylline derivative, mucopolysaccharide.
3. Oil components were added to the water components with continued stirring, without heat.
4. Finally glycols, protein hydrolysate and cellulose thickener were added.

This product provided a basic hair tonic ready for use.

For other products a more concentrated form was prepared which when added to a carrier formulation provided concentrations similar to those provided above. This concentrated hair complex comprised:

Concentrated Hair Stimulant Complex

<u>Component</u>	<u>Concentration</u> <u>(w/w%)</u>
Potassium acetate	0.5
Copper II acetate	0.25
Zinc acetate	0.25
Troloxerutin	0.5

	Theophyllisilane C	5.0
	Dimethyl silanol hyaluronate (available from Exsymol Ltd under the Trade Name "DSH C")	5.0
5	D-Panthenol	2.5
	Silicone Glycol Copolymer (available from Dow Corning under the Trade Name "Dow Corning 193")	7.5
10	Mixture of Zedoary, ginger and cinnamon oil (available from VEVY under the Trade Name "Zedomina")	2.5
	Vitamin A palmitate	0.25
	Vitamin E (available from Henkel under the Trade Name "Copherol F1300")	0.25
15	Onion extract and coconut oil (available from VEVY under the Trade Name "Allum Cepa")	0.5

The order and manner of mixing was as outlined above.

Example 2 Shampoo

- 20 Using the concentrated hair stimulant complex described above, a shampoo is prepared in conventional manner to the following composition:

	<u>Component</u>	<u>Concentration</u> <u>(w/v%)</u>
25	Xanthan Gum (available from Kelco International Ltd under the Trade Name "Keltrol")	0.4
30	Montmorillonite clay (available from English China Clays under the Trade Name "Gel White HNF")	2.0
	Ammonium lauryl sulphate (available from Albright & Wilson under the Trade Name "Empicol AL30T")	10.0

	Sodium laureth sulphate (available from Albright & Wilson under the Trade Name "Empicol ESB 3/Y")	15.0
5	Sodium laureth sulphate (and) glycol distearate (and) cocamide MEA (available from Henkel under the Trade Name "Emperlan L53")	4.0
	Laureth-3 (available from Henkel under the Trade Name "Dehydol LS3")	1.0
10	Polyquaternium-7 (available from Calgon under the Trade Name "Merquat 550")	0.5
	Concentrated Hair Stimulant Complex (see above)	20.0
15	Mixture of glucose, glucose oxidase, lactoperoxidase, sodium iodide and sodium thiocyanate (available from the Boots Co PLC under the Trade Name "Myavert C")	0.9 0.05
	Bronopol	0.02
	Water	to 100

20 Example 3 "Leave-on" Conditioner

Using the concentrated hair stimulant complex described above, a "leave-on" conditioner is prepared in conventional manner to the following composition:

25	<u>Component</u>	<u>Concentration</u> (w/w%)
	Amodimethicone (and) tallow trimonium chloride (and) Nonoxynol 10 (available from Dow Corning under the Trade Name "Cationic Emulsion 929 DC")	1.5
30	Lauryldimonium hydroxypropyl hydrolysed collagen (available from Croda Chemicals under the Trade Name "Croquat L")	1.0
	Cetrimonium chloride (available from Henkel under the Trade Name "Dehyquart A")	2.0

	D-Panthenol 75L	0.2
	Dipropylene glycol	0.24
	Bronopol	0.02
5	Concentrated Hair Stimulant Complex (see above)	20.0
	Water	to 100

CLAIMS

1. The use of one or more of the following as hair stimulants:
 - 5 1) A water-soluble potassium, copper and/or zinc salt, suitably being an acetate salt;
 - 2) A flavone or flavone derivative, suitably comprising rutin, such as troxerutin;
 - 3) A xanthine, such as a theophylline, or a derivative thereof, such as methyl silanol theophyllin acetate
10 alginate;
 - 4) A mucopolysaccharide or derivative thereof such as dimethylsilanol hyaluronate;
 - 5) A fat soluble vitamin or a derivative thereof such as vitamin A (retinol) palmitate or vitamin E
15 (tocopherol);
 - 6) Zedoary, ginger, and/or cinnamon oil; or combinations of these;
 - 7) An allyl-based plant extract such as onion or garlic extract, such as onion extract in coconut
20 oil or garlic extracted in butylene glycol.
2. The use of any one, preferably two or three, of the substances listed in Claim 1 in the manufacture of a medicament for the treatment of hair loss, such as alopecia areata.
- 25 3. A method of treating hair loss (such as alopecia areata) by applying a flavone, a xanthine such as

theophylline or a derivative thereof and at least one, suitably at least two of the other substances listed in Claim 1 to the scalp.

4. A composition for stimulating hair growth and/or
- 5 inhibiting hair loss in humans, comprising a flavone, a xanthine such as theophylline or a derivative thereof and at least one, suitably at least two of the other substances listed in Claim 1, for simultaneous or sequential administration to the scalp.

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